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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/261,329	03/03/1999	KIM VILBOUR ANDERSEN	4887.204-US	7632

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EXAMINER

SLOBODYANSKY, ELIZABETH

ART UNIT PAPER NUMBER

1652

DATE MAILED: 11/05/2002 21

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application N .

09/261,329

Applicant(s)

ANDERSEN ET AL.

Examiner

Elizabeth Slobodyansky

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 June 2002; 20 August 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 79-147 is/are pending in the application.
- 4a) Of the above claim(s) 80-115, 117-135, 137, 138 and 144-147 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 79, 116, 136 and 139-143 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☒ Interview Summary (PTO-413) Paper No(s). 19.
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other:

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DETAILED ACTION

Continued Prosecution Application

The request filed on June 14, 2002 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/218,700 is acceptable and a CPA has been established. An action on the CPA follows.

The AF amendment filed November 21, 2002 amending claims 75 and 76 has been entered.

The amendment filed August 20, 2002 canceling claims 37-78 and adding claims 79-147 has been entered.

Claims 79-147 are pending.

Election/Restriction

This application contains claims directed to the following patentably distinct species of the claimed invention: a modified cellulase of SEQ ID NOs :1-11 mutated at a position selected from the group recited in claim 79 .

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 79, 136, 139, 142 and 143 are generic.

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Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

During a telephone conversation with Mr. Elias Lambiris on August 20, 2002 a provisional election was made with traverse to prosecute the invention of SEQ ID NO:5 mutated at position corresponding to position 119 in SEQ ID NO:1, claims 116, 140, 141. Affirmation of this election must be made by applicant in replying to this Office

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action. Claims 80-115, 117-135, 137, 138 and 144-147 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(l).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 79, with dependent claims 116, 136 and 139-143, is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 79 is directed to a genus of cellulases of SEQ ID NOs : 1-11 having endoglucanase activity comprising one or more mutations at the specific positions

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corresponding to positions of SEQ ID NO:1. Because “comprising “ is open language and “one or more” does not limit the number of mutations, the claim does not impose any structural limitations and reads on any structure that is not necessarily homologous with SEQ ID NO:1 or SEQ ID NO:5.

These claims are directed to a genus of molecules exhibiting endoglucanase activity from any source. The specification teaches the structure of only two representative species of the endoglucanase from *Thielavia terrestris* having the sequence of SEQ ID NO: 5 with the single mutation Q119H or Q119D. The rest of the sequence, 200 amino acids, is identical to SEQ ID NO:5. However, the genus of modified endoglucanases comprises variants additionally mutated at any of said 200 amino acids. Therefore, many functionally and structurally unrelated proteins are encompassed within the scope of these claims, including partial amino acid sequences. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality. This is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

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Claim 79, with dependent claims 116, 136 and 139-143, is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a modified endoglucanase having the structure of SEQ ID NO: 5 mutated at a single position corresponding to residue 119 in SEQ ID NO:1, does not reasonably provide enablement for a modified endoglucanase of SEQ ID NO: 5 comprising said specific mutation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) considered in determining whether undue experimentation is required, are summarized the predictability or unpredictability of the art, and (8) the breadth of the claims.

Claim 79 is directed to a genus of modified endoglucanases comprising one or more specific mutations. Because "comprising " is open language the claim does not impose any structural limitations and reads on any structure that is not necessarily homologous with SEQ ID NO: 5. Therefore, the breadth of these claims is much larger than the scope enabled by the specification.

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The state of the art does not allow the predictability of the properties based on the structure. The specification does not teach which residues besides the specifically mutated are responsible for the resulting properties of the mutant. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of endoglucanases broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired properties/activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and amino acid sequence of a mutant with a substitution at a single position.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to

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modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not teach a rational and predictable scheme for modifying any residues in SEQ ID NO:5 with an expectation of obtaining the desired biological function that is exhibited by a disclosed mutant and the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Therefore, one skilled in the art would require guidance beyond that provided in the specification as to how to make a modified endoglucanase with the amino acid sequence of unknown homology to SEQ ID NO:5. Without such guidance, the experimentation left to those skilled in the art is undue.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 79, with dependent claims 136, 139, 142 and 143 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schulein et al. (A) in view of Schulein et al. (B).

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Schulein et al. (A) (US Patent 6,001,639) teach fungal endoglucanases from various sources including 43 kD endoglucanase from *Humicola insolens* DSM 1800 (column 3, lines 6-27, SEQ ID NO:1 in the instant application). They teach homology among endoglucanases (Figures 1 and 3). They disclose the sequence of endoglucanase from *Thielavia terrestris* (column 42, lines 58-62, SEQ ID NO:12) comprising the sequence of SEQ ID NO:5 of the instant invention.

Schulein et al. (B) (WO 94/07998, form PTO-1449 filed March 3, 1999) teach positions in a cleft comprising the catalytically active site, mutations of which will result in the improved enzymatic activity (page 20, lines 15-20, 29-35). They specifically teach position 119 in 43 kD endoglucanase from *Humicola insolens* DSM 1800 and homologous cellulases (page 21, lines 22-29).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a mutant of SEQ ID NO:5 taught by Schulein et al. (A) that is mutated at position corresponding to residue 119 of SEQ ID NO:1 as suggested by Schulein et al. (B). One skilled in the art would have been motivated to make such a mutant in order to obtain a modified endoglucanase with a different surface conformation of the catalytic cleft resulting in a different interaction pattern between an enzyme and a substrate.

With regard to claim 79, Schulein et al. (B) suggest mutations in a homologous endoglucanase at positions corresponding to positions 4, 5, 6, 7, etc of SEQ ID NO:1.

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For the reasons discussed above, one skilled in the art would have been motivated to make such mutations in SEQ ID NO:5 that is homologous to SEQ ID NO:1.

However, one skilled in the art would have not expected that a specific mutation Q118H in SEQ ID NO:5 that corresponds to mutation at position 119 in SEQ ID NO:1 would result in about 3 fold increase of the enzymatic activity compared with the wild type endoglucanase of SEQ ID NO:5.

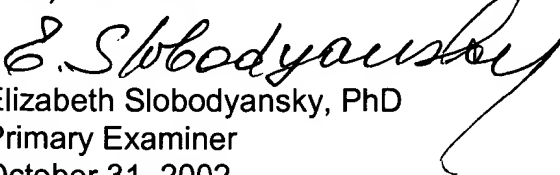
Allowable Subject Matter

Claim drawn to *Thielavia terrestris* Q119H mutant (page 76, lines 16-19), i.e. a mutant with a single mutation Q118H in SEQ ID NO:5 that corresponds to mutation at position 119 in SEQ ID NO:1, would be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.


Elizabeth Slobodyansky, PhD
Primary Examiner
October 31, 2002